

REMARKS

This submission is in response to the Official Action dated March 21, 2003. Claims 10 and 11 have been amended. New claims 12 and 14 have been added. Claims 10-14 are pending and at issue. Consideration of the above identified application, in view of the following remarks, is respectfully requested.

The specification has been amended to include the address for the Korean Collection for Type Cultures at the Korean Research Institute of Bioscience and Biotechnology, and to correct typographical errors in Table 11 on page 31.

Claims 10 and 11 have been amended in matters of formal claim language, *e.g.*, to introduce a period at the end of claim 10, and to remove the recitation of "Yoo" from "*Phellinus linteus* Yoo". Claim 11 has also been amended to independent form.

Additionally, claims 10 and 11 have been amended to recite a biologically pure culture of *Phellinus linteus* strain KCTC 0399BP. This is supported by the specification at, *e.g.*, page 6, lines 23-25. Claim 10 has also been amended to recite that the carbohydrate consists of glucose, mannose, and galactose. This is supported by the specification at, *e.g.*, page 31, Table 11.

New claim 12 recites that the carbohydrate consists of 78.6 mole% glucose, 18.0% mannose, and 3.4 mole% galactose. This is supported by the specification at, *e.g.*, page 31, in Table 11.

New claim 13 recites that the biologically pure culture produces the immuno-stimulating substance when cultured in a culture broth at a pH of 6.0 and a temperature of 28°C for 5 days. This is supported by the specification at, *e.g.*, page 26, lines 3 to 13.

New claim 14 recites the composition of the culture broth in claim 13. This is supported by the specification at, *e.g.*, page 26, lines 3 to 13.

No new matter has been added by way of this amendment.

Statement Under 37 C.F.R. §1.808

It is hereby stated that the deposit of the microorganism given the deposit number KCTC 0399BP was made under the Budapest Treaty, and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent.

Enablement

Claims 10 and 11 stand rejected as allegedly not enabled. Specifically, the Examiner contends that it is not clear that the microorganism is readily available to the public.

In response, a statement pursuant to 37 C.F.R. §1.808, confirming that all restrictions imposed by the depositor on the availability to the public of

KCTC 0399BP will be irrevocably removed upon the granting of a patent has been made in this submission (see above).

Reconsideration and withdrawal of this rejection is therefore respectfully requested.

Indefiniteness

Claims 10 and 11 stand rejected for alleged indefiniteness. Specifically, the Examiner contends that the phrase *Phellinus linteus Yoo* is unclear because of the recitation of "Yoo".

In response, and as suggested by the Examiner, claims 10 and 11 have been amended to no longer recite "Yoo".

Claim 10 has been rejected as indefinite because of the recitation of a polysaccharide substance.

In response, the term "polysaccharide" has been removed.

Claim 11 has been rejected for reciting "perennial", "woody", and other terms which the Examiner contends renders the claim indefinite.

In response, and as suggested by the Examiner, claim 11 has been amended to recite a biologically pure culture of *Phellinus linteus* strain KCTC 0399BP.

In view of the above amendments, reconsideration and withdrawal of these rejections is respectfully requested.

New Matter

Claims 10 and 11 have been rejected as containing new matter. Specifically, the Examiner contends that the recitation of 78.6 mole % mannose and 3.4 mole galactose has no support in the specification.

In response, claim 10 has been amended to recite that the carbohydrate consists of glucose, mannose, and galactose. As previously noted, this is supported by the specification at, *e.g.*, page 31, Table 11.

Therefore, reconsideration and withdrawal of this rejection is respectfully requested.

Non-Statutory Subject Matter

The Examiner has rejected claims 10 and 11 for allegedly reading on a product of nature.

In response, claims 10 and 11 have been amended to recite biologically pure cultures of *Phellineus linteus* strain KCTC 0399BP. This is supported by the specification at, e.g., page 6, lines 23-25.

In view of this amendment, reconsideration and withdrawal of this rejection is respectfully requested.

Anticipation/Obviousness

The Examiner has rejected claims 10 and 11 as allegedly anticipated by, or, alternatively, as allegedly obvious over, Lee et al. [U] or KR 97-15743 [N] in view of U.S. 4,051,314 [IDS-1] and U.S. 4,877,777. Specifically, the Examiner contends that "the polysaccharide substance compositions produced by the same fungal species are reasonably expected to be substantially the same, if not identical, when the same fungal species are cultured at identical culture conditions" (office action, page 12, 1st paragraph). In addition, the Examiner contends that "even if the claimed fungal strain is not identical to the referenced fungal strains with regard to some unidentified characteristics, the difference between that which is disclosed and that which is claimed are considered to be so slight that the references fungal strains are likely to inherently possess the same characteristics of the claimed fungal strain particularly in view of the similar characteristics which they have been shown to share" (office action, page 12, 3rd paragraph).

Applicants respectfully take issue with the Examiner's contentions, because the Examiner has not met the required burden in establishing anticipation by inherency. In order to establish anticipation by inherency, the Examiner must establish that the Lee strain (strain L13202) and the Korean patent strain (strain KCTC 0173BP) necessarily possess the same characteristics of the claimed immuno-stimulating substance, *i.e.*, that the claimed substances are always obtained with the prior art strains. See *In re Robertson*, 169 F.3d. 743, 745 (Fed. Cir. 1999); *Continental Can Co. U.S.A. v. Monsanto Co.*, 948 F.2d 1264 (Fed. Cir. 1991). However, the Examiner has merely indicated that the prior art strains are "likely" or "are reasonably expected" to produce the claimed immuno-stimulating polysaccharide substance. This is not sufficient for establishing inherency, and for this purpose alone, the rejection should be withdrawn.

In the instant case, however, the claimed biologically pure culture of KCTC 0399BP is not only novel, but also unobvious over the cited references. First, the Examiner's attention is respectfully directed to page 19, where Restriction Fragment Length Polymorphism (RFLP) analysis is applied to determine whether KCTC 0399BP is distinct from no less than 11 other *Phellinus* spp. strains. As discussed on page 19, last paragraph:

A phylogenetic tree was inferred from these results and is given as shown in Figure 1, strongly suggesting that the strain of the present invention be newly differentiated from *Phellinus* strains with a significant relatedness.

The Examiner has provided no evidence which would call the distinct nature of the novel strain of the invention into question.

Additionally, it has been found that the immuno-stimulating substance produced by KCTC 0399BP is notably more efficient in evoking an immune response than those produced by other *Phellinus* spp. strains. These findings are presented and discussed below. The experimental findings can also be submitted in form of a Declaration Under 37 C.F.R. §1.132, should the Examiner so prefer.

1. Comparative CD8⁺ T-Lymphocyte-Stimulating Activity:

The ability of the immuno-stimulating substance isolated from KCTC 039BP to stimulate CD8⁺ T-lymphocytes was compared to that of immuno-stimulating substances, *i.e.*, "PL extracts" (see pages 27-28, Example X), isolated from *Phellinus linteus* strains ATCC 26710, 0173BP, and L13202. Strain 0173BP is the strain described by Lee et al [U], and L13202 is the strain described by KR 97-15743. As controls, no substance, PBS, or Concavalin A (ConA) were used. Basically, this test was carried out as outlined in Example XI (pages 28 to 30) and Example XIV (pages 31 to 32), although Fluorescence-Activated Cell-Sorting (FACS) analysis was used for detection of CD8⁺ lymphocytes. See also page 11, line 18 to page 12, line 8.

Briefly, splenocytes were isolated from female Balb/c mice. Cell suspensions were then added to 6-well plates at a concentration of 2×10^6 cells/ml.

Next, PL extract (100 µg/ml) or control (5 µg/ml ConA) was added (one per well) to the wells. The cells were then incubated for 7 days at 37°C in a CO₂ incubator before harvesting, and CD8⁺ T-lymphocytes detected using FACS analysis and a flow cytometer.

The results, depicted in Figure A below, showed that the immunostimulatory substance isolated from KCTC 0399BP resulted in a higher T-lymphocyte activation than those isolated from the other *Phellineus linteus* strains as well as the controls.

CD8 T-lymphocytes Activity of 0399BP (FACS analysis)

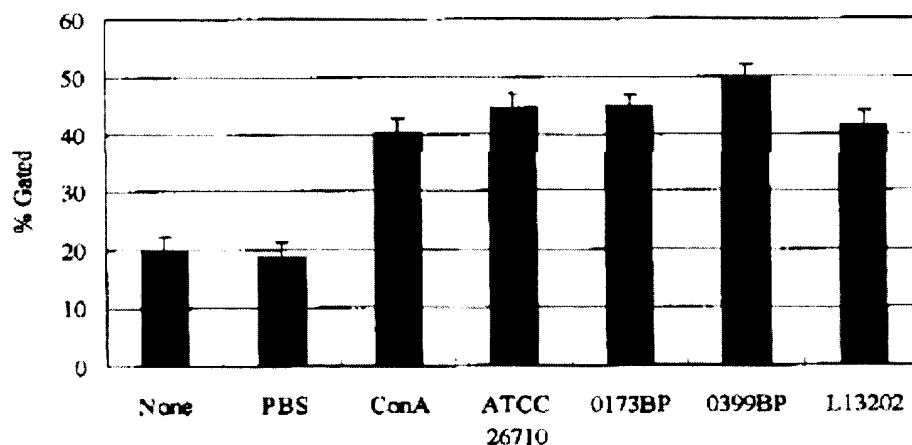


FIGURE A

2. Comparative B-Lymphocyte-Stimulating Activity:

The ability of the immuno-stimulating substance isolated from KCTC 039BP to stimulate B-lymphocyte activity was compared to that of immuno-stimulating substances, "PL extracts", isolated from *Phellinus linteus* strains ATCC 26710, 0173BP, and L13202. Again, strain 0173BP is the strain described by Lee et al [U], and L13202 is the strain described by KR 97-15743. As controls, no substance, PBS, or lipopolysaccharide were used. Basically, this test was carried out as outlined in Example XI (pages 28 to 30) and Example XIV (pages 31 to 32), using an Antibody-Forming Cells (AFC) assay based on haptentation of sheep red blood cells (sRBC). See also page 11, line 18 to page 12, line 8.

Briefly, splenocytes were isolated from female BDF1 mice. Cell suspensions were then added to 48-well plates at a concentration of 5×10^6 cells/ml, in triplicate. Next, PL extract (100 μ g/ml) or control (LPS 25 μ g/ml) was added (one per well) to the wells. The cells were then incubated for 3 days in an atmosphere of 10%CO₂, 7% O₂, and 83% N₂ at 5 psi, before harvesting and counting, and AFC quantified.

The results, depicted in Figure B below, showed that the immuno-stimulatory substance isolated from KCTC 0399BP resulted in a higher portion of antibody-forming B-lymphocytes than those isolated from the other *Phellineus linteus* strains as well as the controls.

B-lymphocytes Activity of 0399BP (AFC assay)

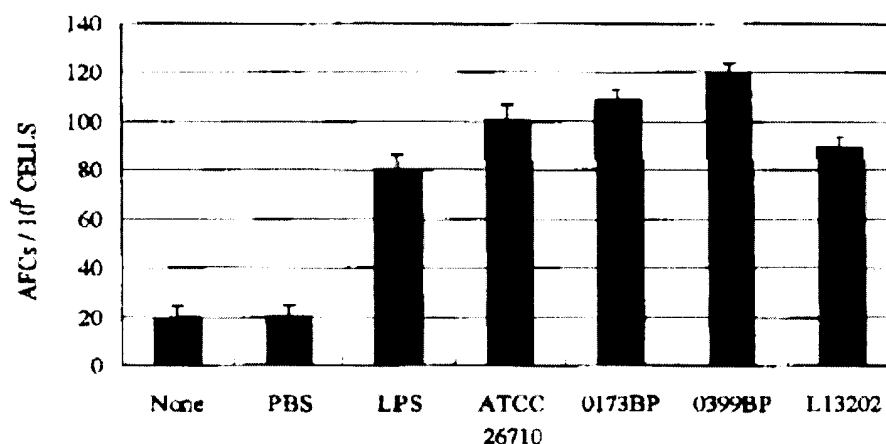


FIGURE B

Thus, the experiments described above verify that the immuno-stimulatory capability of PL extract isolated from KCTC 0399BP is higher than that of other *Phellinus linteus* strains, including ATCC 26710, 0173BP, and L13202. This is not only a surprising and unexpected finding, but also provides for a more efficient use in immuno-stimulatory regimens, such as in the prophylaxis and treatment of immunity-related diseases, due to the superior immuno-stimulating capabilities of the compositions recited in the claims.

As set forth by the MPEP, section 2144.09:

A prima facie case of obviousness based on structural similarity is rebuttable by proof that the claimed

compounds possess unexpectedly advantageous or superior qualities.

See, also, *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963), and *In re Wiechert*, 370 F.2d 927, 152 USPQ 247 (CCPA 1967).

Accordingly, the presently claimed invention is novel and unobvious over the references cited by the Examiner, whether taken alone or in combination. Reconsideration and withdrawal of these rejections is therefore respectfully requested.

* * *

Early and favorable consideration of this response and the claims is earnestly solicited. If there are any other issues remaining which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

Respectfully submitted,



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